Commentary: Surgery expanding to stage IV non-small cell lung cancer treatment?!

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Commentary

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Commentary: Could surgery expand to stage IV non-small cell lung cancer treatment?!

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Central Message

Durable overall survival rates can be achieved in surgically treated oligometastatic NSCLC.

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There is an increasing body of evidence that the overall long-term survival of patients with oligometastatic non–small cell lung cancer (NSCLC) exceeds survival of patients with stage IV disease if all detectable disease is ablated.[1] Depending on the definition of oligometastatic disease (OMD) with numbers of metastases between 1 and 5, the real incidence is not clear and reports range from 16% to 26%.[2,3] The differentiation of this patient group from conventional stage IV patients might be based on a biologically different, more localized state of metastatic disease, but also the fact that advanced radiation techniques, including stereotactic radiotherapy (SABR) and minimal invasive surgery translate into improved disease control. Evidence comes from different randomized controlled trials: in the SABR-Stereotactic Ablative Radiotherapy versus Standard of Care Palliative Treatment in Patients with Oligometastatic Cancers Trial, 18 patients with NSCLC with up to 5 metastases were randomized to SABR or standard of care with a clear advantage for the former in terms of progression free survival.[4] Moreover, Gomez and colleagues conducted a phase 2 study in which 49 patients with up to 3 metastases were randomized to maintenance therapy or local consolidative therapy (LCT), including either radiation, SABR, consolidative chemotherapy, or surgery. The trial was closed early because of clear superiority in the treatment arm, with improved progression-free survival and overall survival.[5] Another phase 2 trial randomized 29 patients with up to 6 metastases to SABR plus maintenance chemotherapy or chemotherapy alone, yielding an increase in progression-free survival.[6] The role of surgery as a LCT modality in OMD for NSCLC is still unclear because only retrospective, albeit robust, data are available showing improved cancer-specific and overall survival.[7-10]

Mitchell and colleagues[11] report the retrospective analysis of NSCLC patients with OMD who underwent comprehensive LCT. The mortality rate of 0% for surgery was associated with a median survival time of 55.2 months compared with 23.4 months after radiotherapy. No differences were observed between modalities in site of first failure, cumulative incidence of locoregional failure, or systemic progression. The authors emphasized that these results should be interpreted in the light of a possible selection bias for the patients for comprehensive LCT. This contribution of Mitchell and colleagues[11] and experts from the MD Anderson Cancer Center Oligometastatic Lung Cancer Working Group further increases the evidence for a role of surgery in patients with stage IV lung cancer with OMD and deserves further investigation in phase 3 clinical trials (as is planned). It will be important for future trials to precisely define OMD and its subclassification—meta- or synchronous and differentiation from oligo recurrence and oligo progression[12]— to obtain comparable results and be based on innovative biomarkers aimed at facilitating unbiased treatment allocation, in particular in the evolving field of immunotherapy as a substantial pillar in the treatment of stage IV

NSCLC.

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